

REMARKS

Claims 25-46 are currently pending in this application. Claims 25, 29, 30, 45 and 46 were withdrawn from consideration in an election filed on March 26, 2009. Claims 26-28 and 31-44 have been examined on the merits and have been rejected under 35 U.S.C. §103(a) as being obvious. In view of the following remarks, removal of the rejections and allowance of claims 26-28 and 31-44 are respectfully requested.

Specification Objections

The Examiner has objected to the specification for informalities that are believed to be addressed in view of the present amendments to the specification. In view of the present amendments, removal of the objections to the specification is respectfully requested.

35 U.S.C. §103(a)

Kamberbeek in view of Furugen, Hogan and Buck

Claims 26-28 and 31-41 are rejected under 35 U.S.C. §103(a) as being obvious over Kamberbeek et al. (J Clin Microbiol, 1997 vol. 35, pp. 907-914) in view of Furugen (Microbial Pathogenesis 2001 vol. 30, pp 129-138), United States Patent No. 5,541,308 to Hogan et al. and Buck et al (Biotechniques (1999) 27(3):528-536) for the reasons indicated on pages 4-8 of the Office Action. Applicants respectfully traverse this rejection.

The invention of claim 26 is directed to method for differentiating Mycobacterium species based on target gene encoding for histone like proteins such as hup β . The method of claim 26 includes obtaining DNA from culture or from clinical samples; amplifying a part of the target gene encoding for histone like proteins such as hup β of Mycobacterium species using said DNA as a template in a polymerase chain reaction with a pair of oligonucleotide primers of SEQ. ID No. 1 and SEQ. ID No. 2; and detecting said amplified fragment of the hup β gene to detect the presence of Mycobacterial species or not and differentiating Mycobacterium tuberculosis from Mycobacterium bovis based on the size of the amplified fragment.

The Examiner applies Kamberbeek to teach the simultaneous detection and differentiation of M. tuberculosis amplification of a DR region with known interspersed space repeats by PCR. The method of Kamberbeek (e.g. spoligotyping) is focused on the examination

and analysis of a Direct Repeat Region (DR Region) in the DNA. The DR Region is not located near the *hupβ* gene in the DNA. Specifically, the DR Region commences from 31, 19, 276 base pair (bp) and stretches up to 31, 23, 484bp; whereas the *hupβ* gene of *M. tuberculosis* (Rv2986c) commences from the 33, 43, 176 base pair and extends up to 33, 43, 820 and the homologue in *M. bovis* is located between bp 32, 99, 736 and 33, 00, 380. As it can be seen, the *hupB* gene of *M. tuberculosis* and its homologue in *M. bovis* are located more than 22,000 bp down stream from the DR Region. Therefore, because the *hupβ* gene of *M. tuberculosis* and its homologue in *M. bovis* are located more than 22,000 bp downstream from the DR Region, it would not have been obvious to one of ordinary skill in the art to assume that similar conclusions and differentiations could be made about the DR Region and the *hupβ* gene of *M. tuberculosis* and its homologue in *M. bovis*.

Additionally, one of ordinary skill in the art would not have known to utilize the size differences in the *hupβ* gene and its homologue in *M. bovis* by examining the DR Region. Particularly, the identification of the differences in gene size of the *hupβ* gene of *M. tuberculosis* (Rv2986c) and its homologue in *M. bovis* (Mbo3010c) provided for the specific design of the primers (SEQ. ID No. 1 and SEQ. ID No. 2). The design of the specific primers used for the differentiation of Mycobacterium species as taught by claim 26, arose through the analysis of the *hupβ* gene of *M. tuberculosis* and its homologue in *M. bovis*. The design of primers specific to the *hupβ* gene of *M. tuberculosis* and its homologue in *M. bovis*, would not have been obvious through the analysis of the upstream genome related to the DR Region.

Therefore, because the *hupβ* gene of *M. tuberculosis* and its homologue in *M. bovis* are not located near the DR Region taught by Kamberbeek and the analysis of the DR Region would not provide the methods including the primers of the claimed invention used for differentiation based on the *hupβ* gene of *M. tuberculosis* and its homologue in *M. bovis*, claim 26 is not obvious in view of Kamberbeek.

Furugen is applied to teach the presence of a DNA binding motif in homologous proteins derived from *M. tuberculosis* and other mycobacterial species, despite variation in size and amino acid content. Particularly, Furugen relates to the function of the DNA binding protein (MDP1) derived from *M. bovis*. The comparative amino acid sequence analysis described by

Furugen shows DNA binding proteins, with variation in amino acid content and number. However, Furugen does not teach or suggest the claimed differentiation and identification of mycobacterial species. Particularly, one of ordinary skill in the art reviewing Furugen would focus on the protein not the exploitation of the differences between the closely related mycobacterial species *M. tuberculosis* and *M. bovis*.

Hogan is applied to teach the use of specific primers.

Buck is applied to teach the equivalence of primers.

However, none of Furugen, Hogan or Buck account for the deficiencies of the teachings of Kamberbeek. Particularly, none of Furugen, Hogan or Buck provides any reason to believe that the method of differentiation based on the DR Region would teach or suggest the claimed primers (SEQ. ID No. 1 and SEQ. ID No. 2) and probes (SEQ. ID No. 7) used to differentiate mycobacterium species based on target gene encoding for histone like proteins. Therefore, Kamberbeek, in view of Furugen, Hogan and Buck does not teach, or suggest each and every element of claims 26 and, therefore, claim 26 is not obvious over the teachings of Kamberbeek in view of Furugen, Hogan and Buck.

Claims 27-28 and 31-41 are depend from and further limit claim 26 and are believed to be patentable for at least the aforementioned reasons. Withdrawal of the rejections under 35 U.S.C § 103(a) and allowance of claim 26-28 and 31-41 are is respectfully requested.

Kamberbeek in view of Furugen, Hogan and Buck, Taylor and Cuende

Claims 42-44 are rejected under 35 U.S.C. §103(a) as being obvious over Kemerbeek et al. in view of Furugen, Hogan et al. and Buck et al as applied to claims 26-28 and 31-41 and further in view of Taylor (J. Clin. Microbiol. 1997, vol. 35 pp. 79-85) and Cuende et al. (Med Clin (Barc) 1995, vol. 104, pp. 207-210) (abstract only) for the reasons set forth on pages 8-10 of the Office Action.

Claims 42-44 depend directly or indirectly from and further limit claim 26. Taylor is applied to teach PCR-restriction fragment length polymorphism to identify 28 species of clinically encountered mycobacteria for identification. Cuende is applied to teach amplification followed by RFLP analysis using HpaII and analysis on gel electrophoresis to generate 13 different patterns to type clinical isolated mycobacteria.

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However, neither Taylor nor Cuende account for the deficiencies of the teachings of Kamberbeek, Furugen, Hogan and Buck. Particularly, neither Taylor nor Cuende provide any reason to believe that the method of differentiation based on the DR Region would teach or suggest the claimed primers (SEQ. ID No. 1 and SEQ. ID No. 2) and probes (SEQ. ID No. 7) used to differentiate mycobacterium species based on target gene encoding for histone like proteins. Therefore, Kamberbeek in view of Furugen, Hogan, Buck, Taylor and Cuende does not teach or suggest each and every element of claims 42-44 and, therefore, claim 42-44 are not obvious over the teachings of Kamberbeek, Furugen, Hogan and Buck. Withdrawal of the rejections under 35 U.S.C §103(a) and allowance of claims 42-44 are respectfully requested.

CONCLUSION

In view of the foregoing, claims 26-28 and 31-44 are patentable over the cited prior art. Accordingly, Applicants respectfully request that claims 26-28 and 31-44 be allowed.

Respectfully submitted,

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